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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,763	11/02/2001	Isaiah J. Fidler	UTSC:684US/SLH	2999

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FULBRIGHT & JAWORSKI L.L.P.
A REGISTERED LIMITED LIABILITY PARTNERSHIP
SUITE 2400
600 CONGRESS AVENUE
AUSTIN, TX 78701

EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,763	FIDLER ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2-14,34-36 and 38-42* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2,3,8-14,34-36 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed October 6, 2005 in response to the Office Action of June 3 is acknowledged and has been entered. Previously pending claims 1, 15-33, 37 and 43 have been cancelled, claims 2-3, 8, 14, 34, 38 have been amended. Claims 2-3, 8-14 and 34-36, 38-41 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 112

4. Claims 2-3, 8-14, 34-36, 38-41 remain rejected under 35 USC 112, first paragraph or the reasons previously set forth in the paper mailed June 3, 2005, Section 6, pages 3-4.

Applicant argues that claim 38 has been placed in independent format and claim 1 has been canceled. Amended claim 38 is now believed to include the elements requested by the Examiner and is now directed to obtaining a non-tumor skin, mucosal or hair follicle tissue by non-invasive means from a patient undergoing the cancer treatment with a chemotherapeutic agent wherein said cancer is growth factor related and expresses a growth factor receptor, and said cancer treatment is directed to said growth factor receptor. Applicant believes that this amendment comports with the Examiner's comments in the action. The argument has been considered but has not been found persuasive because the amendment of claim 38 does not address the issue raised drawn to assaying for the effectiveness of a cancer treatment wherein the cancer expressed growth factor receptor/EGFR prior to treatment.

New Grounds of Rejection

Claim Rejections - 35 USC 112

5. Claims 2-3, 8-14, 34-36, 38-41 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of a cancer that is growth factor related has no clear support in the specification and the claims as originally filed. Applicant has not pointed to support for the newly amended claim limitation and a review of the specification did not reveal support for the newly added claim limitation. The subject matter claimed in claims 2-3, 8-14, 34-36, 38-41 broadens the scope of the invention as originally disclosed in the specification.

6. Claims 2-3, 8-14, 34-36, 38-41 are rejected under 35 USC 112, first paragraph because the specification, while enabling for said method wherein (1) the cancer overexpresses growth factor receptor/EGFR, (2) the method assays growth factor receptor/EGFR phosphorylation before and after treatment with a growth factor receptor/EGFR inhibitor in order to determine the effectiveness of the cancer treatment, does not reasonably provide enablement for said method wherein the cancer expresses a growth factor receptor wherein phosphorylation is determined in the tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of determining the effectiveness of a cancer treatment in a cancer that expresses a growth factor receptor/EGFR comprising determining growth factor receptor/EGFRphosphorylation in a tissue sample obtained by non-invasive procedures. This means determining growth factor receptor phosphorylation in said tissue regardless of whether or not the

growth factor receptor is overexpressed ,and therefore an effective target for the chemotherapeutic, and making a determination of the effectiveness of a cancer treatment without a control that demonstrates the extent of receptor phosphorylation prior to therapy.

The specification teaches that tumor cells generally express more growth factor receptors than normal cells and that chemotherapeutic drugs typically used to treat cancers and their metastases are those that inhibit phosphorylation of the growth factor receptors and include C225 antibody that inhibits phosphorylation of the EGFR (page 2, lines 25-31). Tissue sample types that may be obtained by non-invasive methods include hair follicle cells, buccal mucosa cells, skin scrapings, bladder wash cells, pap-smear samples (p. 3, lines 15-17). The control herein is the amount of growth factor receptor in the sample before the cancer treatment (p. 3, lines 22-25). Applicant exemplifies a method of assaying EGFR phosphorylation from hair follicle wherein parallel expression level of activated EGFR is found both in neoplasms and hair follicles wherein the cancer treatment used targets the EGFR receptor (p. 8, lines 3-5). Applicant teaches that several tumor cell types have been found to express much more growth factor receptors than normal cells and that these receptors are phosphorylated in cancers. Applicant specifically teaches that EGFR has been shown to be highly expressed in human pancreatic tissues wherein administration of PK1166, an EGFR phosphorylation inhibitor, to nude mice results in dramatic shrinkage of metastases of human cancer cells and a reduction in phosphorylated EGFR levels and the present invention takes advantage of this finding to provide a non-invasive method for determining the effectiveness of anticancer agents in treating tumors and metastases (p. 8, lines 18-27). In addition, according to the invention, a sample of EGFR expressing cells is

collected from a patient suffering from a form of cancer which is known to overexpress EGFR prior to treatment and the level of phosphorylation is determined by known methods (p. 9, lines18-30), wherein methods for detection of phosphorylated growth factor receptor are well known in the art (p. 11, lines 4-15), wherein Applicant exemplifies the parallel expression of activated EGFR in Neoplasms and Hair Follicles (see Example 3, pages 60) wherein the exemplified method is not commensurate in scope with the claimed invention because the sample tested is excised (that is by surgical methods, from the skin of the mice used in the experiments).

One cannot extrapolate the teaching of the specification to the scope of the claims because (1) it is not clear from the information in the specification how one would go about determining whether growth factor receptor/EGFR-specific inhibitory therapy was successful if the cancer never over-expressed a growth factor receptor/EGFR prior to treatment since it would not be expected that treatment of a cancer with a growth factor receptor/EGFR phosphorylation inhibitor, wherein said cancer did not overexpress the growth factor receptor/EGFR prior to treatment, would effectively treat a cancer if appropriate concentrations of target were not found on the cancer. Certainly, the specification makes clear that not all cancer types either express or overexpress all growth factor receptors/EGFR (page 8) and further the specification specifically states that the invention is drawn to a patient suffering from a form of cancer which is known to overexpress EGFR prior to treatment (see page 9). Given the above, one would not know how to use the broadly claimed method to determine the effectiveness of a cancer treatment, and because (2) in the absence of a comparison step between before and after treatment it is not possible to determine the effectiveness of the

treatment simply by determining growth factor receptor phosphorylation, rather than by determining the inhibition of receptor phosphorylation as taught by the specification.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention could function as currently claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

7. If Applicant were able to overcome the rejections set forth above, Claims 2-3, 8-14, 34-36, 38-41would still be rejected under 35 USC 112, second paragraph because the claims are drawn to growth factor related cancers. The claims are indefinite as the term "related" is a relative term. The term "related" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. No claims allowed.

9. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT

TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar, PhD
Primary Patent Examiner
December 20, 2005